IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF APPEALS

In re Patent Application of: LI, ET AL.	)	Atty. Docket No.: 5853-376
Serial No.: 10/714,795	)	Group: 3737
Filing Date: 11/17/2003	)	Examiner: Ramirez John F.
Confirmation No.: 2973	)	
For: MULTI-FREQUENCY MICROWAVE-INDUCED THERMOACOUSTIC IMAGING OF BIOLOGICAL TISSUE	)	

APPELLANTS' APPEAL BRIEF UNDER 37 C.F.R. § 41.37

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This is an appeal from the Final Rejection dated March 9, 2006, of claims 1-4, 6-14 & 16, in the above-identified application. The Commissioner is hereby authorized to charge (i) the requisite $250 small entity fee for filing this brief and (ii) the $510 small entity fee for a three month extension of time to Deposit Account 50-0951. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any deficiency or credit any surplus to Deposit Account 50-0951.

37 C.F.R. § 41.37(c)(1)(i) *Real Party in Interest*

The real party in interest in the present appeal is University of Florida Research Foundation, Inc, the assignee of the present application, as recorded in the U.S. Patent and Trademark Office on August 2, 2004, having reel number 015030 and frame number 0727.

37 C.F.R. § 41.37(c)(1)(ii) *Related Appeals and Interferences*

At present there are no related appeals or interferences.

37 C.F.R. § 41.37(c)(1)(iii) *Status of Claims*

Sixteen claims have been filed in the present application. Of these sixteen claims, claims 5 and 15 have been cancelled. All fourteen of the remaining claims stand rejected. The claims on appeal are rejected claims 1-4, 6-14 and 16.

A copy of claims 1-4, 6-14 and 16 involved in this appeal is set forth below in the claims Appendix.

37 C.F.R. § 41.37(c)(1)(iv) *Status of Amendments*

All amendments have been entered in the present application. No amendments were requested in response to the Final Rejection dated March 9, 2006.

37 C.F.R. § 41.37(c)(1)(v) *Summary of Claimed Subject Matter*

Of the claims (1-4, 6-14 and 16) involved in the present appeal, claims 1 and 11 are independent. Independent claim 1 defines the invention in terms of a method, while independent claim 11 defines the invention in terms of a complementary system.

The subject matter of claim 1 recites a method of examining biological tissue 185, and includes the steps of radiating a tissue region 185 with a plurality of microwave radiation pulses which span a range of microwave frequencies of at least 600 MHz. In response to the pulses of microwave radiation, the tissue region 185 emits a plurality of thermoacoustic signals. At least one image of the tissue region 185 is then formed from the plurality of thermoacoustic signals.

Complementary related system claim 11 recites a system 100 for examining biological tissue 185, comprising a microwave radiation source 110 for radiating a tissue region 185 with a plurality of microwave radiation pulses. The plurality of radiation pulses span a range of microwave frequencies of at least 600 MHz. In response to the pulses of microwave radiation, the tissue region 185 emits a plurality of thermoacoustic signals. The system 100 also includes an acoustic transducer array 125 for receiving the thermoacoustic signals, the transducer array 125 providing electrical signals in response to the thermoacoustic signals. The system 100 also includes an imager 160 for forming at least one image of the tissue region from the electrical signals.

Appellants note that the claimed method and system 100 relate to *thermoacoustic imaging* using microwaves, not conventional microwave imaging. In conventional microwave imaging, such as disclosed in the cited Van Veen reference, microwave irradiation of tissue causes the irradiated tissue (e.g. breast tissue) to reflect or scatter, the impinging microwave signals. The microwave signals reflected or scattered from the tissue are received by an antenna which converts the received microwave signal to an electrical signal. Much like visible light, the reflection of microwaves is direction specific. Thus, in conventional microwave imaging, microwave radiation, which by definition is electromagnetic radiation thus consisting of *transverse waves*, having a frequency between 1 and 30 GHz, is irradiated, reflected or scattered by the tissue, detected and analyzed. The specification discusses conventional microwave imaging in paragraphs [0008] through [0010].

In contrast, thermoacoustic imaging analyzes the acoustic (sound) waves generated when tissue 185 irradiated with microwaves is heated and emits acoustic waves, which are non-electromagnetic *longitudinal waves* having a frequency between 20 and 20,000 Hz (this frequency is at least 10^5 times smaller than the frequency of microwaves used for irradiation). The acoustic waves are generated when absorption of the microwave irradiation causes the tissue 185 to heat and expand. The transducer array 125 of the thermoacoustic imaging system receives the acoustic (sound) waves and converts the sound waves into an electrical signal that the imaging device 160 resolves into an image. This, in thermoacoustic imaging, transverse microwaves are irradiated, but longitudinal acoustic waves, which are not electromagnetic waves, are detected by acoustic transducers, such as a piezoelectric based transducer array 125, and analyzed. The specification provides additional discussion of thermoacoustic imaging in paragraphs [0011], [0012] and [0015]-[0017].

In thermoacoustics, the conversion from electromagnetic energy to ultrasound energy is the critical phenomenon that is used for imaging. In addition, because each stimulated tissue region 185 emanates a thermoacoustic signal in all directions, significant complexity is added to resolve the signal received by each transducer in the array 125. Because of the complexity of the conversion from transverse electromagnetic microwaves to longitudinal (non-electromagnetic) acoustic waves, prior to the present invention, there was no disclosure or scientific basis for believing that for thermoacoustic imaging that increasing the bandwidth of the stimulating

electromagnetic radiation would improve the spatial resolution of the image. Thus, to the present invention, the impact of trying a wide range of microwave stimulating frequencies was unknown for thermoacoustic imaging, except for the obvious computational complexity which by itself would strongly teach way from using a wide range of frequencies. In fact, the computational complexity of resolving the signals generated by multiple frequencies was recognized in the cited Kruger reference as the basis for using a single microwave frequency for generating thermoacoustic images.

Prior to the claimed invention, the areas investigated for improving spatial resolution in thermoacoustic imaging focused on the aperture and the number of transducers of the transducer array, *see* Specification, paragraph [0017]. Other areas of research included specific discrete microwave frequencies and pulse duration, *see* Specification, paragraph [0017]. The fact a multiple irradiation frequencies was unknown for improving spatial resolution is also clearly evidenced in the Wang reference (U.S. Patent No. 6,567,688), which is disclosed in the application and was previously cited by Examiner. Wang teaches that the "lateral resolution is determined by the numerical aperture of the ultrasonic transducer," Wang, col. 10, ln. 4-5; see Wang, col. 10, ln. 4-20 (as used in Wang, lateral resolution corresponds to spatial resolution, while axial resolution corresponds to tissue depth). Prior to the time of the invention, a thermoacoustic researcher seeking to generate images with improved spatial resolution would have avoided multiple frequencies and thus looked solely to optimization of the transducer array. Thus, without the benefit of impermissible hindsight, one having ordinary skill in the art at the time of the present invention would have had no motivation to even look to a multiple irradiation frequencies, multiple irradiation frequencies being clearly far removed from the claimed microwave frequency range of 600 MHz.

Specifically, the data set provided by stimulating electromagnetic radiation over the claimed ultra wideband range of frequencies is obviously quite large as compared to the data provided by conventional single frequency stimulation. The present specification describes methods for the highly complex task of forming images from such a large amount of data spread over the claimed ultra wideband frequency range. These methods include using a *significant and non-obvious modification* of a preferred adaptive beamformer, the Robust Capon Beamformer (RCB). The original RCB is disclosed in an article by one of the present inventors entitled "On

robust Capon beamforming and diagonal loading." In fact, the RBC method was filed as U.S. Patent Application No. 10/358,597, and subsequently issued as U.S. Patent No. 6,798,380. Specifically, the present inventors discovered how to utilize the large data set collected from a plurality of different stimulating frequencies, such as to form a single image, using a non-obvious modification of RCB, as described in paragraph 62 (copied below).

> [00062] Application specific factors for thermoacoustic imaging according to the invention require extending the RCB algorithm to wideband signals. As disclosed in U.S. Application No. 10/358,597, the RCB algorithm is generally described for narrowband signal. To extend the RCB for application to wideband signals, a wideband signal can be divided into several narrowband frequency bins, and the RCB applied to each bin. Thus, the relatively wideband thermoacoustic signal can be treated as comprising a plurality of narrow pulses with the arrival time and pulse duration approximately known. Through time gating, a large portion of signal interferences can be removed before applying the RCB.

The improved spatial resolution achieved using Robust Capon Beamforming when compared to conventional delay-and-sum procedures and standard Capon Beamforming, is shown in Figure 3. These methods are discussed in specification paragraphs [0057]-[0062].

The following is a correlation of the subject matter of independent claims 1 and 11 and dependent claim 8 by parenthetical reference to the drawings and associated descriptions in the specification.

Claim 1

1. A method of examining biological tissue 185, comprising the steps of:

radiating a tissue region 185 with a plurality of microwave radiation pulses **(Specification paragraph [0022])**, said plurality of radiation pulses spanning a range of microwave frequencies of at least 600 MHz **(Specification paragraph [0035])**, wherein said tissue region 185 emits a plurality of thermoacoustic signals **(Specification paragraph [0024], [0025], [0038]; Figure 3)** responsive to said plurality of microwave pulses, and

forming at least one image **(Specification paragraph [0024], [0050], [0058], [0060]-[0063])**of said tissue region from said plurality of thermoacoustic signals **(Specification paragraph [0024], [0025], [0038]; Figure 3)**.

Claim 8

8. The method of claim 1, wherein said pulses include a plurality of different polarizations **(Specification, p. 7, ln. 17; paragraphs [0052]-[0053)**.

Claim 11

11. A system for examining biological tissue 185, comprising:

a microwave radiation source 110 **(Specification paragraph [0042])** for radiating a tissue region 185 with a plurality of microwave radiation pulses **(Specification paragraph [0022])**, said plurality of radiation pulses spanning a range of microwave frequencies of at least 600 MHz **(Specification paragraph [0035], [0036])**, wherein said tissue region 185 emits a plurality of thermoacoustic signals **(Specification paragraph [0024], [0025], [0038]; Fig. 3)** responsive to said microwave pulses;

an acoustic transducer array for receiving said thermoacoustic signals, said transducer array 125 **(Specification paragraph [0046]-[0048])** providing electrical signals in response thereto, and

an imager 160 **(Specification paragraph [0050])**for forming at least one image **(Specification paragraph [0024], [0050], [0058], [0060]-[0063])** of said tissue region from said electrical signals.

37 C.F.R. § 41.37(c)(1)(vi) *Grounds of Rejection to be Reviewed on Appeal*

Claims 1-4, 8, 11-14 and 16 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kruger (U.S. Patent No. 6,104,942) in view of Van Veen *et al.* (U.S. Patent Publication No. 2003/0088180).

Claims 6, 7, 9 and 10 16 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kruger (U.S. Patent No. 6,104,942) in view of Van Veen *et al.* (U.S. Patent Publication No. 2003/0088180), further in view of Bolstad et al. (U.S. Patent No. 5,630,154).

37 C.F.R. § 41.37(c)(1)(vii) *Argument*

The deficiencies of the rejection of claims 1-4, 11-14 and 16 under 35 U.S.C. § 103(a) as being unpatentable over Kruger in view of Van Veen et al.

Claims 1-4

According to the Examiner:

Kruger teaches a method of and apparatus for examining biological tissue including radiating a region of tissue with microwave radiation pulses that span a range of microwave frequencies, where the tissue region emits thermoacoustic signals responsive to the microwave pulses that are received by an acoustic transducer array that may be mechanically moved, which then provides electrical signals in response, and where the radiation pulses are produced by at least one antenna and include a plurality of polarizations, and forming at least one image of the tissue region from the thermoacoustic signals, where the at least one image comprises a plurality of images from fractional portions of the tissue that are combined to form an overall image (col. 1, lines 13-15, col. 3, lines 1-30, col. 4, lines 3-32, 42-51 and 63-67, col. 5, lines 1-45 and 60-67 and col. 6, lines 1-7). Kruger does not explicitly teach that the range of microwave frequencies is at least 600 MHz or at least 1 GHz, that the tissue region is breast tissue and that the at least one antenna is a horn antenna.

In the same field of endeavor of microwave imaging of tissue, Van Veen et al. teaches the use of ultrawideband microwave frequencies to image breast tissue, where the microwave radiation is produced by a horn antenna (paras. 3, 5, 29 and 43). Although Van Veen et al. uses the applied microwave radiation for traditional microwave imaging by receiving the microwave energy reflected by the tissue, the application of microwave energy would inherently cause the heating of tissue that produces the thermoacoustic signals as in Kruger. Thus, one of ordinary skill in the art would understand that the radiation applied by Van Veen et al. could be used for

thermoacoustic imaging. Further, it would have been obvious to one of ordinary skill in the art at the time of the invention that applying a wider range of frequencies results in more information collected, and thus improved images of the tissue. As Kruger teaches the application of microwave energy swept across a range of frequencies, it would have been obvious to use the ultrawideband frequencies of Van Veen et al. in order to maximize the detail in the information collected.

Appellants respectfully disagree with the above characterization of the Kruger reference as well as the obviousness rejection asserted above. In particular, the Examiner's assertion that Kruger teaches "microwave pulses that span a range of frequencies" is clearly erroneous. In addition, neither Kruger nor the knowledge in the art at the time of the present invention provide the necessary motivation to modify Kruger to use pulses, or to use a range of microwave frequencies. However, before reviewing the claim rejections based on cited art, Appellants will review the features of the claimed invention as recited in claim 1.

Claim 1 recites a method of examining biological tissue 185 that includes the steps of irradiating a tissue region 185 with a plurality of microwave radiation pulses which span a range of microwave frequencies of at least 600 MHz, wherein the tissue region 185 emits a plurality of thermoacoustic signals in response. At least one image of the tissue region 185 is then formed from the plurality of thermoacoustic signals.

As noted above, in thermal acoustics, impinging microwave (electromagnetic) waves radiation (frequency between 1 and 30 GHz) is absorbed by tissue 185, which generates longitudinal acoustic (sound) waves (frequency between 20 and 20,000 Hz) that are received and used to generate an image. Prior to the claimed invention, the impact of trying a range of irradiation frequencies, such as the claimed ultra wideband range of frequencies, was unknown for thermoacoustic imaging, except for the obvious computational complexity which by itself would strongly teach away from its consideration.

Significantly, prior to the present invention, it was believed that resolution in thermoacoustic imaging could only be improved by adjusting the transducer array's aperture and the number of transducers, *see* Specification, paragraph [0017]. This is confirmed by the Wang reference (U.S. Patent No. 6,567,688, cited by the Examiner in the Office Action mailed September 7, 2005), which teaches that the "lateral resolution is determined by the numerical aperture of the ultrasonic transducer," Wang, col. 10, ln. 4-5; see Wang, col. 10, ln. 4-20 (as used in Wang, lateral resolution corresponds to spatial resolution and axial resolution corresponds to tissue depth). Other areas of research for improving spatial resolution included specific microwave frequencies and pulse duration, *see* Specification, paragraph [0017]. Thus, thermoacoustic researchers seeking to generate images with improved resolution would have had no suggestion or motivation to use multiple frequency pulses, let alone the claimed wideband range of 600 MHz, in order to improve spatial resolution.

Turning now to the cited art, the primary cited reference, Kruger, discloses methods and an apparatus for measuring and characterizing the localized electromagnetic wave absorption properties of biologic tissues *in vivo*, using incident electromagnetic waves to produce resultant acoustic waves. The tissue is exposed to modulating electromagnetic radiation, to produce modulating acoustic signals. The modulating acoustic signals are detected by an acoustic sensor which is primarily sensitive to acoustic radiation at a focal point distant from the sensor.

Kruger discloses two embodiments, both of which rely on *continuously modulating electromagnetic radiation*, such as sinusoids, **not pulses, pulses being clearly discontinuous**. The first embodiment creates a thermoacoustic image by combining multiple measurements taken from multiple different focal points. The second embodiment is used to generate an absorption spectrum, not a thermoacoustic image, for a specific point by taking several measurements of the focal point while slowly sweeping the frequency of the electromagnetic irradiation. As will be explained in more detail below, the absorption embodiment is clearly not thermoacoustics and does not even hint at the use of an ultra wideband frequency range of at least 600 MHz. Kruger discloses that either of these embodiments may be useful for medical diagnostic purposes.

The first Kruger embodiment (thermoacoustic imaging) is a method of imaging tissue by irradiating the tissue with *continuously modulating electromagnetic radiation*, and detecting the resulting acoustic waves as disclosed in Kruger, col. 3 lines 12-21:

> Specifically, in one embodiment, the invention features a method of imaging tissue structures from localized absorption of electromagnetic waves, by irradiating the tissue with *continuously modulating electromagnetic radiation*, and detecting the resulting acoustic waves with an acoustic sensor which is primarily sensitive to acoustic radiation at a first focal point distant from the sensor. The sensor is used to collect data from two or more different locations in the tissue, and this data is combined to produce an image of structures in the tissue.

Although the passage above discloses continuously modulating electromagnetic radiation, it does not say what is being modulated: phase, frequency, or amplitude. The description of the RF signal generator used therein provides the answer. The Kruger RF signal generator includes a "carrier frequency generator operating at a frequency ω, whose *amplitude* will be modulated periodically by a modulator 11b in response to a modulating signal at a much lower frequency f_o, $f<<\omega$ generated by a source 11c. The [amplitude] modulation may be sinusoidal, square wave, or any other shape," Kruger, col. 4, ln. 5-11. Clearly, the modulation in Kruger's first embodiment deals with the amplitude of the microwaves, not the frequency. This amplitude modulation is further evidence of Kruger's teaching of a single fixed microwave frequency.

The reason Kruger does not modulate the irradiation frequency (thus holding frequency constant) when producing thermoacoustic images becomes apparent upon review of the mathematics used by Kruger, *see* Kruger, col. 6, ln. 9- col. 8, ln. 48. Kruger notes that because the microwave frequency, ω, is constant, "only pressure waves of frequency, f_o, are produced within the tissue volume," *see* Kruger, col. 7-9. It was acknowledged in Kruger that this significantly decreases the noise and simplifies the associated equipment and the process of resolving the data:

> *Since the effective bandwidth of the detection circuitry 50, 52, 53 is determined by the time constant of the low-pass filter 54, extremely low bandwidth circuitry can be used* in control circuit 53, adjustment circuit 50 and demodulating amplifier 52 while remaining primarily sensitive to the modulation frequency f_o of the radiation source. The net result is a

> dramatic decrease in the detector's electronic noise compared to the wide-bandwidth detector required with pulsed acquisition devices such as that disclosed in the above-referenced U.S. Patent. For these devices the bandwidth of the detection system is on the order of $2f_o$, where f_o is the center frequency of the transducer. *Assuming that the time constant of the low-pass filter is 1 second, the electronic noise will be reduced by a factor of* $(2 f_o)^{1/2}$ *or 1400 for* f_o*=1MHz compared to a pulsed acquisition system.* This is an important property of the thermoacoustic localization methodology of the present invention.

Kruger, col. 8, ln. 32-48.

As noted previously, the above reference to the constant modulation frequency f_o of the radiation source refers to the modulation frequency of the amplitude, and not frequency modulation, see Kruger, col. 4, ln. 4-10. This passage teaches that using a single fixed frequency and continuous microwave radiation allows the use of low bandwidth circuitry, thereby reducing signal noise by a factor of 1400 compared with the wide-bandwidth detectors required for acquisition of pulsed radiation. Thus, the above passage in Kruger provides an additional teaching that strongly discourages the use of more than one microwave frequency or microwave pulses, the combination of both, both being recited in the claimed invention.

The second Kruger embodiment (absorption spectrum of individual focal points) again uses continuous, frequency modulating electromagnetic radiation generated by the source, and the resultant longitudinal (compression) waveforms arriving at the acoustic sensor from the focal point, which are compared to the frequency of the electromagnetic radiation to form a measure of the absorptivity spectrum as disclosed in col. 3, lines 22-30:

> In a second embodiment, a similar apparatus is used in characterizing tissue at a focal point of the acoustic sensor. In this embodiment, continuous, frequency modulating electromagnetic radiation is generated by the source, and the resultant pressure waveforms arriving at the acoustic sensor from the focal point, are compared to the frequency of the electromagnetic radiation, to form a measure of the absorptivity spectrum of tissue located at the focal point of the acoustic sensor.

A comparison of the two Kruger embodiments is copied below:

> In use, the focus point of transducer 30 may be scanned about the inside of the tissue sample 24, while collecting signal amplitude data from amplifier 34. The amplitude data can then be plotted as a grey-scale as a function of

> focal point position to form a two- or three-dimensional image of the tissue structures. Alternatively, *if the microwave frequency is swept slowly (compared to tau) over time across some range of values while the focal point is maintained, an absorption spectrum for the tissue at the focal point* of the transducer will be generated over time. This spectrum can be displayed by PC 38 on display terminal 40 and used to characterize the tissue at the focal point. These techniques can be combined to generate two- or three-dimensional images reflecting absorptivity spectra at multiple focal points.

Kruger, col. 5 line 60 to col. col. 6, line 7

Although Appellants acknowledge that taken out of the context the above Kruger disclosure regarding the absorption embodiment may appear to refer to using a potentially significant range of microwave frequencies based on the disclosed microwave frequency being "swept", a review of the entire Kruger disclosure demonstrates that Kruger does not disclose or suggest the frequency being swept for thermoacoustics imaging or the claimed 600 MHz range of frequencies for the absorption embodiment. Specifically, Kruger discloses that "if the *microwave frequency is swept slowly (compared to* τ*)* over time across some range of values while the focal point is maintained, an absorption spectrum for the tissue at the focal point of the transducer will be generated over time," Kruger, col. 5, ln. 65-col. 6, ln. 2. Thus, the range of frequencies disclosed by Kruger for the absorption embodiment cannot be fully understood without considering Kruger's disclosure with respect to τ, the time constant of the low-pass filter.

Kruger discloses that the "output of the demodulating amplifier is fed to a low-pass filter, ***whose time constant*** τ is chosen to be much greater than $1/f_o$," Kruger, col. 8, ln. 18-20. From the previous discussion it should be clear that f_o refers to the modulation frequency of the amplitude of the microwave radiation use for irradiation, Kruger, col. 4, ln. 4-10, and that τ is the time constant of the low pass filter in the detection circuit, Kruger, col. 8, ln. 18-20.

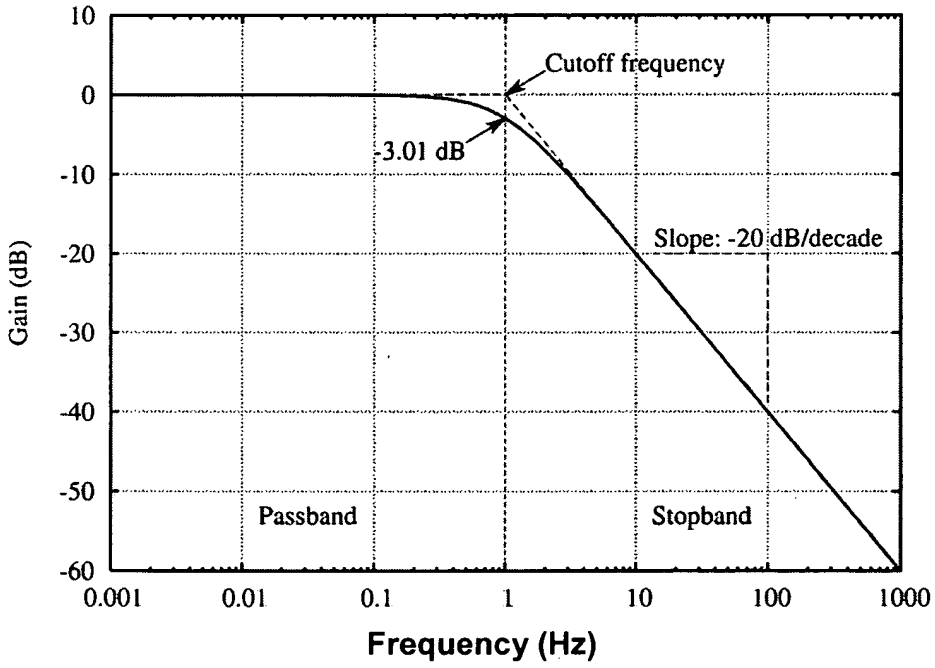
Kruger goes on to disclose:

> For these devices [detection circuits] the bandwidth of the detection system is on the order of $2f_o$, where f_o is the center frequency of the transducer. *Assuming that* ***the time constant of the low-pass filter is 1 second****, the electronic noise will be reduced by a factor of* $(2 f_o)^{1/2}$ *or 1400 for* f_o*=1MHz compared to a pulsed acquisition system.* This is an important property of the thermoacoustic localization methodology of the present invention.

As indicated in the passage above, a low-pass filter is used to remove noise from the electrical signal output by the acoustic transducer array. Low-pass filters are well known to be used to eliminate frequencies above a cutoff frequency, f_c. The cutoff frequency, f_c, is calculated using the following equation:

$$f_c = \frac{1}{2\pi\tau} = \frac{1}{2\pi RC}$$

In the above equation, τ which equal RC, is the time constant of low-pass filter. Thus, the cutoff frequency f_c can be calculated from the time constant τ. Kruger's only disclosure of a time constant (τ) is 1 second as noted above, which corresponds to a cutoff frequency of 0.159 Hz [f_c=1/(2*π*1)] for processing the electrical signal. An illustrative Bode plot of a low-pass filter with a cutoff frequency of 1.0 Hz is shown below.



Significantly, Kruger discloses that an absorption spectrum may be obtained "if the microwave frequency is swept slowly (compared to τ) over time across some range of values which the focal point is maintained," Kruger, col. 5, ln. 65 – col. 6, ln. 2. Some calculations provided below will emphasize the significance of this result with respect to the range of frequencies disclosed. A frequency sweep based on τ=1 second would be equal to 0.159 Hz = 0.159 cycles per second. Since there are 3,600 seconds in an hour, a frequency sweep based on

τ=1 second would span approximately 575 Hz in an hour. Thus, sweeping the 600 MHz range of the claimed invention would take about 1.05 million hours, or 119 years, to complete. Clearly, an image that takes 119 years to generate would not be useful for medical diagnostics and would not disclose or suggest the claimed 600 MHz range of frequencies.

In the same paragraph, Kruger discloses an amplitude modulation frequency, f_o, of 1 MHz. If 1 MHz is used as the cutoff frequency f_c, $\tau = 0.0001592$ seconds. This amounts to a swept span of 22.619 MHz per hour. Thus, sweeping the 600 MHz range of the claimed invention would take about 26.5 hours, or more than one day to complete. Clearly, an image that takes more than one day to generate would not be useful for the intended medical diagnostic use and would not disclose or suggest the claimed 600 MHz range of frequencies.

However, Kruger does not disclose a method that would take one day or even 1 hour and 20 minutes to complete a sweep of the claimed 600 MHz range. Kruger teaches that the "*microwave frequency is swept slowly (compared to τ) over time*," Kruger, col. 5, ln. 65-66. Assuming "slowly" is at least 5 times slower that τ, ***the claimed 600 MHz range of the claimed invention would take five days to generate using the numbers disclosed in the Kruger disclosure***. Clearly, Kruger does not disclose or suggest the claimed 600 MHz frequency range for use as a medical diagnostic tool since no person skilled in the art (or otherwise) would use a 600 MHz frequency range when it would take 5 days or more to generate an image. This powerfully teaches away from combining Kruger with any reference disclosing the claimed 600 MHz range of frequencies. Moreover, as noted above, Kruger's frequency sweeping is only disclosed for absorption, not the thermoacoustics.

Having firmly established that Kruger teaches away from the claimed 600 MHz frequency range, Appellants point out that Kruger also teaches away from pulses. The Examiner asserts that Kruger "teaches a method and apparatus for examining biological tissue including radiating a region of tissue *with microwave radiation pulses that span a range of microwave frequencies*." Appellants respectfully point out that ***Kruger does not disclose or suggest use of irradiating pulses***. In both thermoacoustic and absorption embodiments, Kruger discloses continuous periodically modulated radiation, such as continuous sinusoids, as opposed to pulses. Moreover, Kruger strongly teaches away from using irradiating pulses by noting the continuously periodically modulated radiation "substantially increase[s] the signal-to-noise ratio

of the recorded signal, reduce[s] the power requirements of the radiation source, and simplify[ies] the reconstruction methodology and the complexity of the associated apparatus," *see* Kruger, col. 3, ln. 7-11. This teaching away from pulses is clearly reinforced in Kruger, col. 2 line 66 to col. 3 line 11 (copied below):

> The present invention improves upon what is disclosed by Bowen and in the above-referenced U.S. Patent Application in several ways. First, the present invention uses *continuous, periodically modulated radiation in place of narrowly pulsed radiation.* Continuous radiation can be used to stimulate sonic waves continuously without having to wait for sequences of pulses. The localizing method for reconstructing uses constructive and destructive interference of periodic sonic waves generated by the *continuous radiation.* This approach can substantially increase the signal-to-noise ratio of the recorded signal, reduce the power requirements of the radiation source, and simplify the reconstruction methodology and the complexity of the associated apparatus.

Since Kruger teaches continuous radiation "can substantially increase the signal-to-noise ratio of the recorded signal, reduce the power requirements of the radiation source, and simplify the reconstruction methodology and the complexity of the associated apparatus" as compared to pulsed radiation, Kruger clearly teaches away from methods based on pulsed-microwaves, such as the invention claimed by Appellants. Standing alone, the absence of pulsed microwave radiation in Kruger defeats the prima facie case of obviousness asserted by the Examiner.

Forgetting for the moment Kruger's clear failure to disclose pulsed irradiation and Kruger's teaching away from pulsed microwave irradiation, as noted above, the Examiner attempts to use Van Veen to make up for Kruger's deficiency with regard to Appellants' claimed method of examining biological tissue comprising use of a "plurality of microwave radiation pulses, said plurality of radiation pulses spanning a range of microwave frequencies of at least 600 MHz" for stimulating the tissue.

Appellants note that the claimed method and system relate to *thermoacoustic imaging* which is based on analysis of induced *acoustic* (sound waves are <u>not</u> electromagnetic waves). In both thermoacoustic imaging and conventional microwave imaging, microwaves irradiation interacts with tissue. Some of the microwaves are reflected by the tissue, others are absorbed and still others simply pass through. The difference is which aspect of the interaction between microwave radiation and tissue is measured. In conventional microwave imaging, such as

disclosed in the cited Van Veen reference, microwave radiation, having a frequency between 1 GHz and 30 GHz, that is reflected by the tissue is received by an antenna and the emanated microwave signal is converted to an electrical signal. In contrast, in the claimed thermoacoustic imaging, the tissue absorbs the microwave radiation thereby generating thermoacoustic signals which are non-electromagnetic waves, having a frequency between 20 and 20,000 Hz, which are collected by an acoustic transducer, such as a piezoelectric based transducer array 125, which converts the sound waves to an electrical signal. The unpredictable transformation from a transverse microwave (electromagnetic) signal with a frequency of 1 to 30 GHz into a longitudinal acoustic (non-electromagnetic) signal with a frequency between 20 and 20,000 Hz adds significant complexity to the task of resolving the data, particularly where multiple microwaves over an ultra wideband range are irradiated in a pulse.

Van Veen discloses microwave imaging via space-time beamforming carried out by transmitting microwave signals from multiple antenna locations into an individual to be examined and receiving the backscattered (reflected) microwave signals at multiple antenna locations. The received signals are processed in a computer to remove the skin interface reflection component of the signal at each antenna to provide corrected signal data. The corrected signal data is provided to a beamformer process that time shifts the received signals to align the reflected component from a scatterer at a candidate location, and then passes the time aligned signals through a bank of filters, the outputs of which are summed, time-gated and the power therein calculated to produce the beamformer output signal at a candidate location. The beamformer is then scanned to a plurality of different locations in the individual by changing the time shifts, filter weights and time-gating of the beamformer process. The output power may be displayed as a function of scan location, with regions of large output power corresponding to significant microwave scatterers such as malignant lesions, see Van Veen Abstract.

Appellants note that the ultra wideband microwave stimulation disclosed by Van Veen is well-known in the radar community. In Van Veen, it is the reflected microwave radiation wave that is used to form tumor images. Van Veen thus clearly relates to conventional microwave imaging where microwaves are transmitted to the tissue and microwaves are received by the detector/imager. In the Van Veen reflection-based approach, the wider the bandwidth, the better the range resolution. As noted above, for the thermoacoustics disclosed in the first Kruger

embodiment and the claimed invention, it is the conversion from EM energy to ultrasound energy that is used for imaging. As discussed above prior to the present invention, the transducer array's characteristic aperture and number of transducers were the only system parameters known to improve the spatial image of the image. Accordingly, the Examiner's asserted motivation for using Van Veen's ultrawide pulses with Kruger's invention by "applying a wider range of frequencies results in more information collected, and thus improved images of the tissue ... to maximize the detail in the information collected" is only half true. While it is true that the asserted motivation does generally result in more information collected, prior to the present invention the thermoacoustic imaging art believed that the detail collected using different frequencies was simply different and the spatial resolution of the image of the tissue was not improved.

Moreover, as noted above, the impact of trying a wide range of frequencies was unknown for thermoacoustics prior to the present invention, except for the obvious computational complexity which by itself would strongly teach way from its consideration as taught by Kruger who teaches improvement over Bowen (narrow pulsed-based thermal acoustics) by instead using *continuous, periodically modulated radiation in place of narrowly pulsed radiation because:*

> Continuous radiation can be used to stimulate sonic waves continuously without having to wait for sequences of pulses. The localizing method for reconstructing uses constructive and destructive interference of periodic sonic waves generated by the *continuous radiation*. This approach can substantially increase the signal-to-noise ratio of the recorded signal, reduce the power requirements of the radiation source, and simplify the reconstruction methodology and the complexity of the associated apparatus.

Kruger, col. 2, ln. 66 – col. 3, ln. 11.

Accordingly, since there is no motivation to combine Van Veen with Kruger there cannot be a prima facie case of obviousness. Moreover, as noted above, Kruger's continuous microwave irradiation at a single frequency for all of Kruger's thermoacoustic embodiments clearly teaches away from Appellants' claimed method of examining biological tissue by radiating a tissue region with a plurality of microwave radiation pulses that span a 600 MHz range of microwave frequencies. Even for Kruger's absorption embodiment (which is not thermoacoustic) which recites a swept frequency, as demonstrated above the sweeping is so slow that a range of even 1

KHz would take more than 1 hour. Therefore, Appellants submit that claims 1 and 10 and their respective dependent claims are patentable over Kruger and/or other thermoacoustic art in view of Van Veen.

The following fact findings by the E.P. Examiner in the corresponding PCT case amount to a full rebuttal of the U.S. Examiners analysis and is fully consistent with Appellant's arguments. While not binding on a U.S. Examiner, these conclusions should be given substantial weight since they are based on a cogent analysis of the cited art including Kruger and the previously cited Wang reference. Appellants refer to a copy of the International Preliminary Report on Patentability (IPRP) rendered by the EPO and submitted with Appellants' reply to Office Action Filed June 2, 2006 (note that Appellants incorrectly identified the IPRP as the "Search Report/Written Opinion" in the Reply to Final Office Action). The IPRP focused on PCT application claims 1 and 10, which are identical to claims 1 and 11 at issue in this Appeal. The cited references included Kruger (referred to as D2) and Wang (referred to as D1). Inventive step was found for all claims. Reasons for such finding are copied below:

> **Reference is made to the following documents:**
> **D1: US6567688 B**
> **D2: US6104942 A**
>
> **Document D1, which is considered to represent the most relevant state of the art,** discloses a method and apparatus for examining biological tissue by scanning electromagnetically-induced thermoacoustic tomography.
>
> **The subject-matter of the independent claims 1 and 10 differs in that the tissue region** is radiated with a plurality of microwave radiation pulses, said plurality of radiation pulses spanning a range of microwave frequencies of at least 600 MHZ.
>
> **This difference forms a solution to the problem of** enhancing thermoacoustic imaging of biological tissue, e.g. gathering more information about tissue regions and permitting detection of smaller tumors.

Contrary to the current independent claims, document D1 teaches use of a single microwave pulse frequency generally in the range from 300 MHz to 3 Ghz (D1, col. 5, lines 22-30).

Document D2 teaches two embodiments for imaging: thermoacoustic (see especially D2, col. 3, lines 12-21) and absorption spectrum (see especially D2, col. 3, lines 22-30). In both embodiments, continuos periodically modulated radiation is employed (see also D2, col. 2, line 66-col. 3, line 11). Furthermore, document D2 only teaches a narrowband frequency range and seems not to disclose or suggest forming an image from thermoacoustic signals obtained by using a range of stimulating frequencies. In the single embodiment where document D2 does disclose sweeping of the microwave frequency (e.g. D2, col. 5, line 60-col. 6, line 11), there is no hint to the use of an ultrawideband frequency range of at least 600 MHz.

The specific features of the solution provided by claim 1 are neither disclosed in nor rendered obvious by either one of the available citations. As a consequence, the person skilled in the art, who set off to solve the aforementioned problem starting from the disclosure of document D1 or D2, would not find any indications or prompts in the available prior art documents to modify the method and system for examining biological tissue in the way set out in the independent claims. The solution proposed in these claims of the present application is therefore considered as involving an inventive step.

As noted in the International Preliminary Report on Patentability (IPRP), Wang (U.S. Patent 6,567,688), not Kruger, is considered the most relevant state of the art. An obviousness rejection based on Wang was made in the Office Action dated September 7, 2005. As noted in the Final Office Action of March 9, 2006, Appellants current claims are distinguishable from Wang (see Final Office Action, page 2, paragraph 2).

The IPRP notes that both Kruger (referred to as "Document D2") embodiments employ continuous periodically modulated radiation. The IPRP then points out that Kruger discloses only a narrowband frequency range and does not disclose or suggest forming an image from thermoacoustic signals obtained by using a range of stimulating frequencies. Even where Kruger discloses sweeping of microwave frequencies for creating an absorption spectrum, which is not thermoacoustics, "there is no hint to the use an ultrawideband frequency range of at least 600 MHz."

The E.P. Examiner's conclusions that Kruger fails to disclose or suggest using a range of frequencies for generating an image reinforces Appellants' arguments concerning lack of motivation and a teaching away.

In summary, while Kruger deals with thermoacoustic imaging using continuous irradiation in his first embodiment, Kruger does not disclose or suggest using a range of frequencies in the thermoacoustic embodiment. Although, Kruger's absorption embodiment (which is not thermoacoustic) does once mention a "swept slowly" frequency, the "swept slowly" is with respect to a time constant of the low-pass filter in the detection circuit, where as noted above, calculates to less than a 1 kHz range in one hour, much less the 600 MHz wideband range of frequencies of the claimed invention. Appellants have also demonstrated that prior to the present invention, the knowledge of those skilled in the art of thermoacoustics taught away from the use of multiple irradiation frequencies since it was believed that only characteristics of the transducer array determined spatial resolution in the image. Accordingly, there was no motivation, suggestion or teaching, to combine Kruger with Van Veen in any manner that would result in the claimed invention (i.e. add ultra wideband frequency microwave radiation).

In addition, Kruger's thermoacoustic method deals only with continuous fixed frequency microwave irradiation, not pulses. Thus, the Examiner's position that Kruger teaches "microwave radiation pulses that span a range of microwave frequencies" is clearly erroneous. The Van Veen teaching is applicable to conventional microwave imaging, not thermoacoustic microwave imaging. Thus, Kruger's strong teaching away from pulses is not cured by Van Veen's use of pulses in a technology that is clearly distinct from conventional microwave imaging in physics, methodology, and required instrumentation. Accordingly, Kruger's powerful teaching away from pulses cannot be cured by the Van Veen reference which is unrelated to thermoacoustics.

Reversal of the rejection of claim 1-4 is respectfully requested.

Claims , 11-14 and 16

Independent claim 11 and dependent claims 12-14 and 16 are drawn to the complementary system of independent method claim 1. Appellants reassert the arguments made with respect to claims 1-4 with respect to claims 11-14 and 16.

Reversal of the rejection of claim 11-14 and 16 is respectfully requested.

The deficiencies of the rejection of claim 8 under 35 U.S.C. § 103(a) as being unpatentable over Kruger in view of Van Veen et al.

Claim 8 delimits claim 1, by specifying that the pulses include a plurality of different polarizations. As noted in the specification, since cancerous tumors are generally non-spherical in shape, thermoacoustic signals emitted by such tumors are generally polarization sensitive, *see* Specification paragraph [0052]-[0053]. Polarization may be achieved by rotation of a TEM horn antenna.

The Examiner asserts that Kruger discloses polarization. However, Appellants thorough review of the Kruger reference did not turn up any references to polarization. In addition, Appellants reassert the arguments made with respect to claims 1-4, 11-14 and 16 with respect to claim 8.

Reversal of the rejection of claim 8 is respectfully requested.

The deficiencies of the rejection of claims 6, 7, 9 and 10 under 35 U.S.C. § 103(a) as being unpatentable over Kruger in view of Van Veen et al., further in view of Bolstad

Appellants reassert the arguments made with respect to claims 1-4, 11-14 and 16 with respect to claims 6, 7, 9 and 10.

Reversal of the rejection of claims 6, 7, 9 and 10 is respectfully requested.

CONCLUSION

For the reasons advanced in the foregoing, Appellants respectfully submit that the invention defined in claims 1-4, 8, 11-14 and 16 is not rendered obvious by Kruger in view of Van Veen and respectfully request that the rejection thereof on such ground be reversed.

For the Appellants respectfully submit that the invention defined in claims 6, 7, 9 and 10 is not rendered obvious by Kruger in view of Van Veen further in view of Bolstad and respectfully request that the rejection thereof on such ground be reversed.

37 C.F.R. § 41.37(c)(1)(viii) *Claims Appendix*

1. A method of examining biological tissue, comprising the steps of:

radiating a tissue region with a plurality of microwave radiation pulses, said plurality of radiation pulses spanning a range of microwave frequencies of at least 600 MHz, wherein said tissue region emits a plurality of thermoacoustic signals responsive to said plurality of microwave pulses, and

forming at least one image of said tissue region from said plurality of thermoacoustic signals.

2. The method of claim 1, wherein said tissue region comprises breast tissue.

3. The method of claim 2, wherein said at least one image of said breast tissue comprises a plurality of said images, said plurality of images from fractional portions of said breast, further comprising the step of combining said images from said local regions to form an overall image of said breast.

4. The method of claim 1, wherein said frequency range is at least 1 GHz.

6. The method of claim 1, wherein said step of forming at least one image comprises adaptive beamforming.

7. The method of claim 6, wherein said adaptive beamforming comprises the steps of:

providing a sensor array including a plurality of sensor elements, wherein an array steering vector corresponding to a signal of interest (SOI) is unknown;

representing said array steering vector with an ellipsoidal uncertainty set;

bounding a covariance fitting relation for said array steering vector with said uncertainty ellipsoid, and

solving said covariance fitting relation to provide an estimate of said array steering vector.

8. The method of claim 1, wherein said pulses include a plurality of different polarizations.

9. The method of claim 1, further comprising the step of pattern recognition from said image.

10. The method of claim 9, wherein said step of pattern recognition comprises adaptive signal processing.

11. A system for examining biological tissue, comprising:

a microwave radiation source for radiating a tissue region with a plurality of microwave radiation pulses, said plurality of radiation pulses spanning a range of microwave frequencies of at least 600 MHz, wherein said tissue region emits a plurality of thermoacoustic signals responsive to said microwave pulses;

an acoustic transducer array for receiving said thermoacoustic signals, said transducer array providing electrical signals in response thereto, and

an imager for forming at least one image of said tissue region from said electrical signals.

12. The system of claim 11, further comprising at least one horn antenna coupled to said microwave radiation source for emanating said plurality of microwave pulses.

13. The system of claim 12, further comprising structure for translating at least one of said transducer array and said antenna.

14. The system of claim 11, wherein said plurality of radiation pulses span a frequency range of at least 1 GHz.

16. The system of claim 11, wherein said pulses include a plurality of different polarizations.

_____/

37 C.F.R. § 41.37(c)(1)(ix) *Evidence Appendix*

Appellants submit herewith, International Preliminary Report on Patentability rendered by the European Patent Office on February 3, 2006, already of record.

_____/

37 C.F.R. § 41.37(c)(1)(x) *Related Proceedings Appendix*

There are no related proceedings.

Respectfully submitted,

AKERMAN SENTERFITT

Date: February 12, 2007

Neil R. Jetter
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P.O. Box 3188
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Tel: 561-653-5000

Docket No. 5853-376

3/17/06

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Jetter, Neil R.
AKERMAN SENTERFITT
222 Lakeview Avenue, 400
West Palm Beach, FL 33402
ETATS-UNIS D'AMERIQUE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	03.02.2006
Applicant's or agent's file reference: 5853-376WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2004/036670	03.11.2004	17.11.2003

Applicant
UNIVERSITY OF FLORIDA ET AL

FEB - 6 2006

AKERMAN SENTERFITT, P.A.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Viegas da Cruz, I Tel. +31 70 340-1923

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
5853-376WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2004/036670	03.11.2004	17.11.2003

International Patent Classification (IPC) or national classification and IPC

A61B5/05

Applicant

UNIVERSITY OF FLORIDA ET AL.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14.09.2005	03.02.2006

Name and mailing address of the international preliminary examining authority:

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Lommel, A

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/036670

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-22	as originally filed
Claims, Numbers	
1-15	filed with the demand
Drawings, Sheets	
1/3-3/3	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-15
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-15
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:
D1: US6567688 B
D2: US6104942 A

Document D1, which is considered to represent the **most relevant state of the art**, discloses a method and apparatus for examining biological tissue by scanning electromagnetically-induced thermoacoustic tomography.

The **subject-matter of the independent claims 1 and 10 differs in that** the tissue region is radiated with a plurality of microwave radiation pulses, said plurality of radiation pulses spanning a range of microwave frequencies of at least 600 MHZ.

This **difference forms a solution to the problem of** enhancing thermoacoustic imaging of biological tissue, e.g. gathering more information about tissue regions and permitting detection of smaller tumors.

Contrary to the current independent claims, document D1 teaches use of a single microwave pulse frequency generally in the range from 300 MHz to 3 Ghz (D1, col. 5, lines 22-30).

Document D2 teaches two embodiments for imaging: thermoacoustic (see especially D2, col. 3, lines 12-21) and absorption spectrum (see especially D2, col. 3, lines 22-30). In both embodiments, continuos periodically modulated radiation is employed (see also D2, col. 2, line 66-col. 3, line 11). Furthermore, document D2 only teaches a narrowband frequency range and seems not to disclose or suggest forming an image from thermoacoustic signals obtained by using a range of stimulating frequencies. In the single embodiment where document D2 does disclose sweeping of the microwave frequency (e.g. D2, col. 5, line 60-col. 6, line 11), there is no hint to the use of an ultrawideband frequency range of at least 600 MHz.

The specific features of the solution provided by claim 1 are neither disclosed in nor rendered obvious by either one of the available citations. As a consequence, the person skilled in the art, who set off to solve the aforementioned problem starting from the disclosure of document D1 or D2, would not find any indications or prompts in the available prior art documents to modify the method and system for examining biological tissue in the way set out in the independent claims. The solution proposed in these claims of the present application is therefore considered as **involving an inventive step.**

[SUBSTITUTE SHEET]

CLAIMS

We claim:

1. A method of examining biological tissue, comprising the steps of:

radiating a tissue region with a plurality of microwave radiation pulses, said plurality of radiation pulses spanning a range of microwave frequencies of at least 600 MHz, wherein said tissue region emits a plurality of thermoacoustic signals responsive to said plurality of microwave pulses, and

forming at least one image of said tissue region from said plurality of thermoacoustic signals.

2. The method of claim 1, wherein said tissue region comprises breast tissue.

3. The method of claim 2, wherein said at least one image of said breast tissue comprises a plurality of said images, said plurality of images from fractional portions of said breast, further comprising the step of combining said images from said local regions to form an overall image of said breast.

4. The method of claim 1, wherein said frequency range is at least 1 GHz.

5. The method of claim 1, wherein said step of forming at least one image comprises adaptive beamforming.

[SUBSTITUTE SHEET]

6. The method of claim 5, wherein said adaptive beamforming comprises the steps of:

providing a sensor array including a plurality of sensor elements, wherein an array steering vector corresponding to a signal of interest (SOI) is unknown;

representing said array steering vector with an ellipsoidal uncertainty set;

bounding a covariance fitting relation for said array steering vector with said uncertainty ellipsoid, and

solving said matrix fitting relation to provide an estimate of said array steering vector.

7. The method of claim 1, wherein said pulses include a plurality of different polarizations.

8. The method of claim 1, further comprising the step of pattern recognition from said image.

9. The method of claim 8, wherein said step of pattern recognition comprises adaptive signal processing.

10. A system for examining biological tissue, comprising:

a microwave radiation source for radiating a tissue region with a plurality of microwave radiation pulses, said plurality of radiation pulses spanning a range of microwave

[SUBSTITUTE SHEET]

frequencies of at least 600 MHz, wherein said tissue region emits a plurality of thermoacoustic signals responsive to said microwave pulses;

an acoustic transducer array for receiving said thermoacoustic signals, said transducer array providing electrical signals in response thereto, and

an imager for forming at least one image of said tissue region from said electrical signals.

11. The system of claim 10, further comprising at least one horn antenna coupled to said microwave radiation source for emanating said plurality of microwave pulses.

12. The system of claim 11, further comprising structure for translating at least one of said transducer array and said antenna.

13. The system of claim 10, wherein said frequency range is at least 1 GHz.

14. The system of claim 10, wherein said microwave radiation source generates ultrawideband signals.

15. The system of claim 10, wherein said pulses include a plurality of different polarizations.